

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

TAKENOUCHI, KAZUYA, et al.

Divisional of Appln. No.: 09/830,167
Filed April 23, 2001

Group Art Unit: Not Yet Assigned

Confirmation No.: Not Yet Assigned

Examiner: Not Yet Assigned

Filed: January 4, 2002

For: VITAMIN D3 DERIVATIVE AND TREATING AGENT FOR INFLAMMATORY
RESPIRATORY DISEASE USING SAME

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination, please amend the above-identified application as follows:

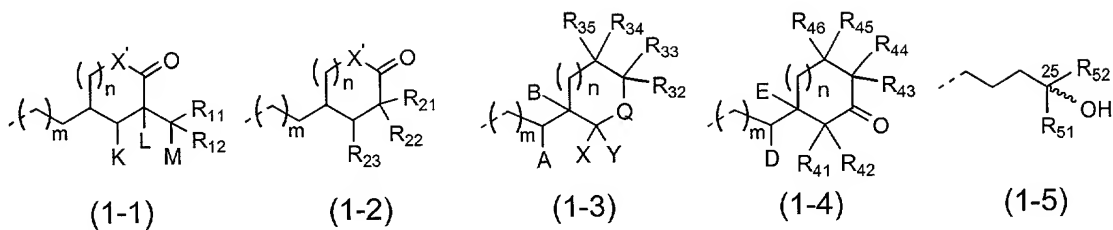
IN THE SPECIFICATION:

Amend the specification by inserting before the first line the sentence:

This is a Divisional of Application No. 09/830,167 filed April 23, 2001, the disclosure of
which is incorporated herein by reference.

**Page 6, please delete the paragraph at lines 18-19 with formulas (1-1) to (1-5), and
replace it with the following new paragraph:**

204010 " 010402
10035551 010402

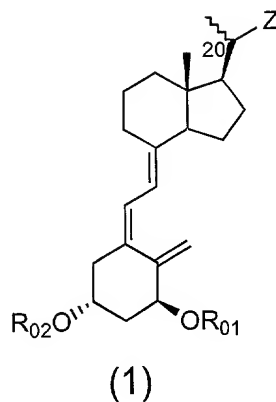


IN THE CLAIMS:

Please cancel claims 1-44

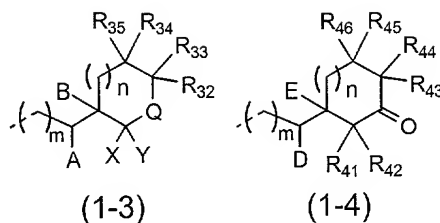
Please enter new claims 45-61:

45. A vitamin D₃ derivative expressed by the following general formula (1) or pharmaceutically permissible solvates thereof,



{wherein, R₀₁ and R₀₂ are each independently a hydrogen atom, a trimethylsilyl group, a triethylsilyl group, a t-butyldimethylsilyl group, an acetyl group, a methoxymethyl group or a tetrahydro-4H-pyran-2-yl group;

Z is one out of the following formulae (1-3) and (1-4),



[in the above formulae (1-3) and (1-4),

m is an integer of 0 to 2;

n is an integer of 0 to 2;

R₃₂, R₃₃, R₃₄ and R₃₅ are identical to or different from each other, and they are a hydrogen atom, a hydroxyl group, a C₁-C₄ alkyl group or a C₂-C₅ acyloxy group;

A and B are identical to or different from each other, and they express a hydrogen atom or a hydroxyl group, or together express a single bond and form a double bond in cooperation with the single bond already shown in the formula;

X and Y together express a carbonyl group in cooperation with the carbon atom to which they are bonded, one of them is a hydrogen atom and the other is a hydroxyl group, or one of them is a hydrogen atom and the other is a C₂-C₅ acyloxy group;

R₄₁ and R₄₂ are identical to or different from each other, and they express a hydrogen atom, a hydroxyl group, a trifluoromethyl group, a pentafluoroethyl group, a C₂-C₅ acyloxy group, a C₁-C₄ alkyloxy group or a C₁-C₄ alkyl group which may be substituted with a hydroxyl group, a C₂-C₅ acyloxy group or a C₁-C₄ alkyloxy group, or both the members together express a C₁-C₅ alkylidene group, or they express a C₃-C₆ cyclic alkyl group in cooperation with the carbon atom to which they are bonded;

R₄₃ and R₄₄ are identical to or different from each other, and they express a hydrogen atom, a hydroxyl group, a trifluoromethyl group, a pentafluoroethyl group, a C₂-C₅ acyloxy group, a C₁-C₄ alkyloxy group or a C₁-C₄ alkyl group which may be substituted with a hydroxyl group, a C₂-C₅ acyloxy group or a C₁-C₄ alkyloxy group, or both the members together express a C₁-C₅ alkylidene group, or express a C₃-C₆ cyclic alkyl group in cooperation with the carbon atom to which they are bonded;

R₄₅ and R₄₆ are identical to or different from each other, and they express a hydrogen atom, a hydroxyl group, a trifluoromethyl group, a pentafluoroethyl group, a C₂-C₅ acyloxy group, a C₁-C₄ alkyloxy group or a C₁-C₄ alkyl group which may be substituted with a hydroxyl group, a C₂-C₅ acyloxy group or a C₁-C₄ alkyloxy group;

D and E express each a hydrogen atom, D is a hydroxy group and E expresses a hydrogen atom, D and E together express a single bond and express a double bond in cooperation with the single bond already shown in the formula, or E and R₄₁ together express a single bond and express a double bond in cooperation with the single bond already shown in the formula, wherein D expresses a hydrogen atom or a hydroxy group; and R₄₂ expresses a hydrogen atom, a hydroxyl group, a trifluoromethyl group, a pentafluoroethyl group, a C₂-C₅ acyloxy group, a C₁-C₄ alkyloxy group or a C₁-C₄ alkyl group which may be substituted with a hydroxyl group, a C₂-C₅ acyloxy group or a C₁-C₄ alkyloxy group,]

with the proviso that the following compound (a) is excluded,

(a) a compound in which the groups of one combination out of R_{32} and R_{33} , R_{34} and R_{35} , R_{41} and R_{42} , R_{43} and R_{44} , and R_{45} and R_{46} are both hydroxy groups, both alkyloxy groups, or a hydroxy group and an alkyloxy group.))}

46. A vitamin D_3 derivative or a pharmaceutically permissible solvate thereof described in Claim 45, wherein, in the above formula (1), Z is (1-3)

47. A vitamin D_3 derivative or a pharmaceutically permissible solvate thereof described in Claim 45, wherein, in the above formula (1), Z is (1-4).

48. A vitamin D_3 derivative or a pharmaceutically permissible solvate thereof described in one out of Claims 45, 46 and 47, wherein, in the above formula (1), R_{01} and R_{02} are both hydrogen atoms.

49. A vitamin D_3 derivative or a pharmaceutically permissible solvate thereof described in one out of Claims 45, 46 and 47, wherein, in the above formula (1), m is 0 or 1.

50. A vitamin D_3 derivative or a pharmaceutically permissible solvate thereof described in one out of Claims 45, 46 and 47, wherein, in the above formula (1), n is 0 or 1.

51. A vitamin D_3 derivative or a pharmaceutically permissible solvate thereof described in Claim 46, wherein, in the above formula (1), Q is $>C(-F)-R_{31}$.

52. A vitamin D_3 derivative or a pharmaceutically permissible solvate thereof described in Claim 46, wherein, in the above formula (1), Q is $>N-R_{31}$.

53. A vitamin D_3 derivative or a pharmaceutically permissible solvate thereof described in Claim 46, wherein, in the above formula (1), R_{31} is a hydrogen atom, a hydroxyl

group or a C₁-C₄ alkyl group which may be substituted with a hydroxy group, a C₂-C₅ acyloxy group or a C₁-C₄ alkyloxy group.

54. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 46, wherein, in the above formula (1), R₃₂, R₃₃, R₃₄ and R₃₅ are each a hydrogen atom.

55. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 46, wherein, in the above formula (1), A and B are both hydrogen atoms, A is a hydroxyl group and B is a hydrogen atom, or A and B together express a single bond and form a double bond in cooperation with the single bond already shown in the formula.

56. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 46, wherein, in the above formula (1), X and Y together express a carbonyl group in cooperation with the carbon atom to which they are bonded.

57. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 47, wherein, in the above formula (1), R₄₁ and R₄₂ are both hydrogen atoms or together express a methylene group.

58. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 47, wherein, in the above formula (1), R₄₃ and R₄₄ are both hydrogen atoms or together express a methylene group.

59. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 47, wherein, in the above formula (1), R₄₅ and R₄₆ are both hydrogen atoms.

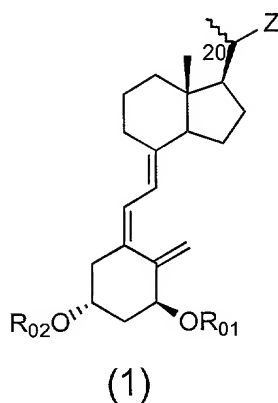
60. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 47, wherein, in the above formula (1), D and E are both hydrogen atoms, D and E together express a single bond and form a double bond in cooperation with the single bond already shown in the formula, or D is a hydrogen atom and E and R₄₁ together express a single bond and express a double bond in cooperation with the single bond already shown in the formula.

61. A pharmaceutical composition composed of a vitamin D₃ derivative or pharmaceutically permissible solvate thereof described in claim 45 and a pharmaceutically permissible carrier.

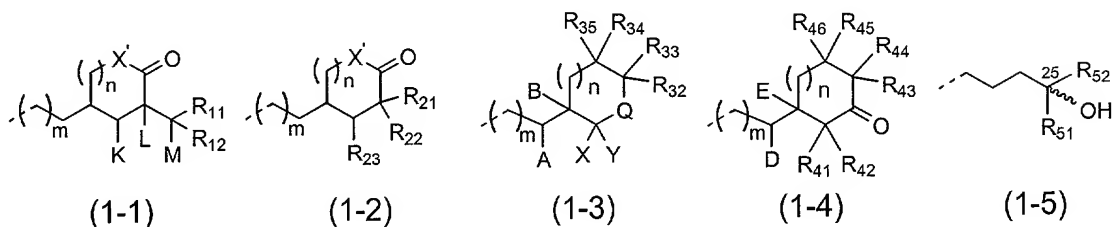
IN THE ABSTRACT OF DISCLOSURE:

Please delete the present Abstract of the Disclosure and replace it with the following new Abstract of the Disclosure:

Compounds expressed by the following general formula (1),



[wherein, R_{01} and R_{02} are each independently a hydrogen atom or a protecting group for a hydroxyl group; Z is one out of the following formulae (1-1) to (1-5)].



The compounds can be used as active ingredients of treating agents for inflammatory respiratory diseases, malignant tumors, rheumatoid arthritis, osteoporosis, diabetes mellitus, hypertension, alopecia, acne, psoriasis, dermatitis, hypercalcemia, hypoparathyroidism and metabolic disorder of cartilage.

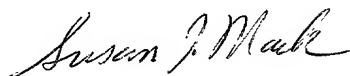
REMARKS

The specification and the Abstract have been amended to correct an inadvertent error in formulae (1-1) and (1-2) for Z, wherein X in the formulae has been changed to X'. The basis for the change can be seen in the subsequent disclosure of X' at, e.g., page 7, line 1, and the overall disclosure at, e.g., page 6, line 18 to page 7, line 9 in the application.

Claims 45-61 correspond to original claims 1-32 and 44 amended to meet the limitations of the compounds of group VI defined in the Restriction Requirement issued October 4, 2001 in parent application 09/830,167.

Entry of the above amendment is respectfully requested.

Respectfully submitted,



Susan J. Mack
Registration No. 30,951

SUGHRUE MION, PLLC
2100 Pennsylvania Avenue, N.W.
Washington, D.C. 20037-3213
Telephone: (202) 293-7060
Facsimile: (202) 293-7860
Date: Jan. 4, 2002

APPENDIX

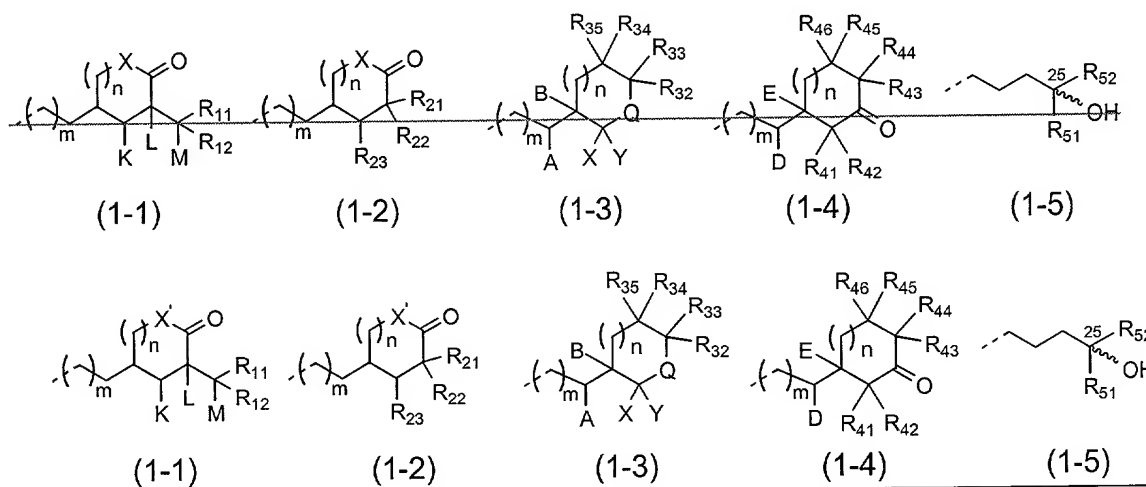
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Amend the specification by inserting before the first line of the sentence:

This is a Divisional of Application No. 09/830,167 filed April 23, 2001, the disclosure of which is incorporated herein by reference.

Page 6, the paragraph at lines 18-19 with formulas (1-1) and (1-5):



IN THE CLAIMS:

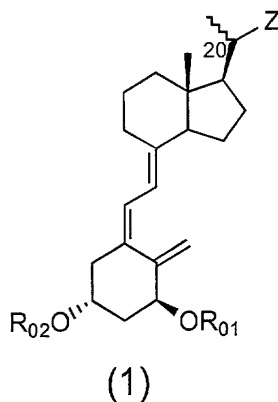
Please delete claims 1-44.

Please add new claims 45-61.

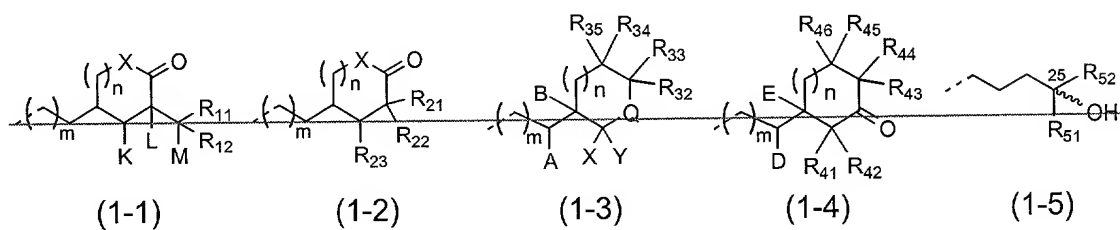
IN THE ABSTRACT OF DISCLOSURE:

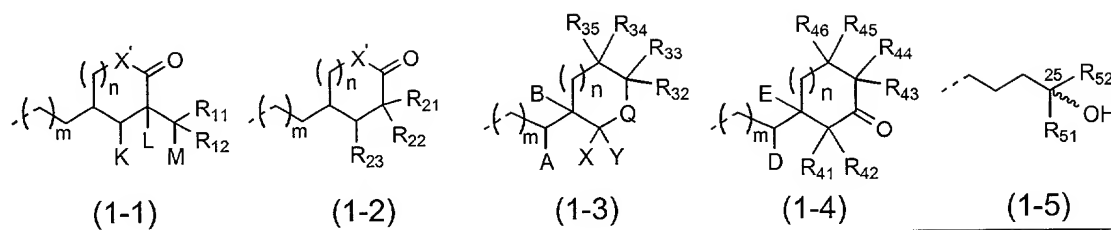
The abstract is changed as follows:

Compounds expressed by the following general formula (1),



[wherein, R_{01} and R_{02} are each independently a hydrogen atom or a protecting group for a hydroxyl group; Z is one out of the following formulae (1-1) to (1-5)].





The compounds can be used as active ingredients of treating agents for inflammatory respiratory diseases, malignant tumors, rheumatoid arthritis, osteoporosis, diabetes mellitus, hypertension, alopecia, acne, psoriasis, dermatitis, hypercalcemia, hypoparathyroidism and metabolic disorder of cartilage.